Catalysis and covalent binding energies of antibodies

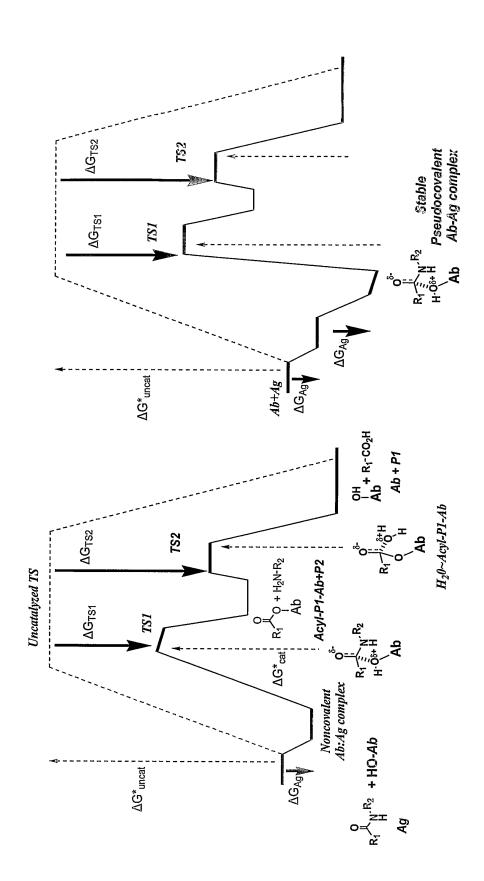
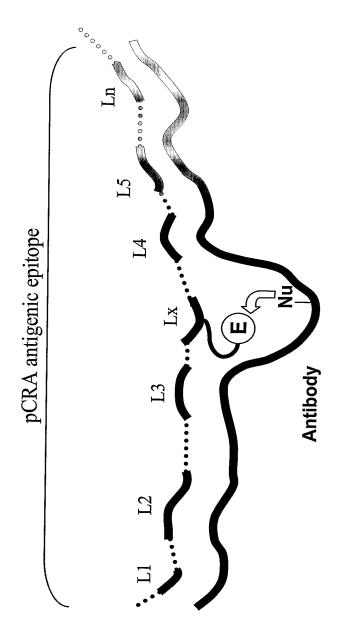


Fig 1



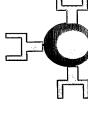


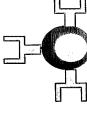
Induction of catalyst synthesis

Ordinary polypeptide antigen, Slow transmembrane signal

Aborted clonal selection,

tolerance

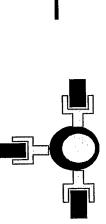








Increased turnov⊜r, pro⊪ration





Rabid ∜ransmembrane signal Covalent stimulation,

L' =sulfhydryl group of Cys

General structure of pCRA

• L'-Y"-Y'-Y, Example

• L'-Y"-Y, Example 3

L¹.Y"."¥'."¥, Example 2

$$V'' = \gamma - \text{male imidobutyryl group}$$

$$V'' = \gamma - \text{male imidobutyl group}$$

$$V'$$

pCRA Z-R pair: Example 1

A. Electron withdrawing substituents with peptide extension

B. Electron donating substituents with peptide extension

Selected examples of metal binding moiety

- 1. (His)n
- 2. (Cys-Aaa-Cys-Cys): metallothionein αdomain-derived peptide
- 3. (Cys-Aaa-Cys): metallothionein β-domainderived peptide 4. EDTA
- 5. a crown ether6. DAMP

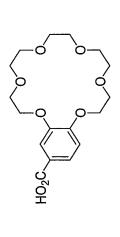
Example of 2: Cys-Ser-Cys-Cys

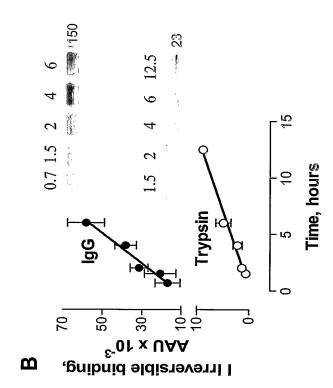
Example of 3: Cys-Ser-Cys

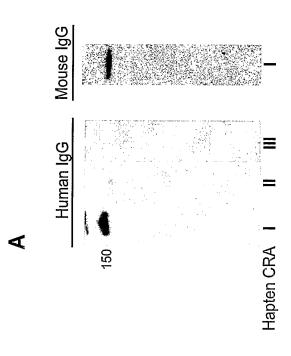
Example of 6: DAMP

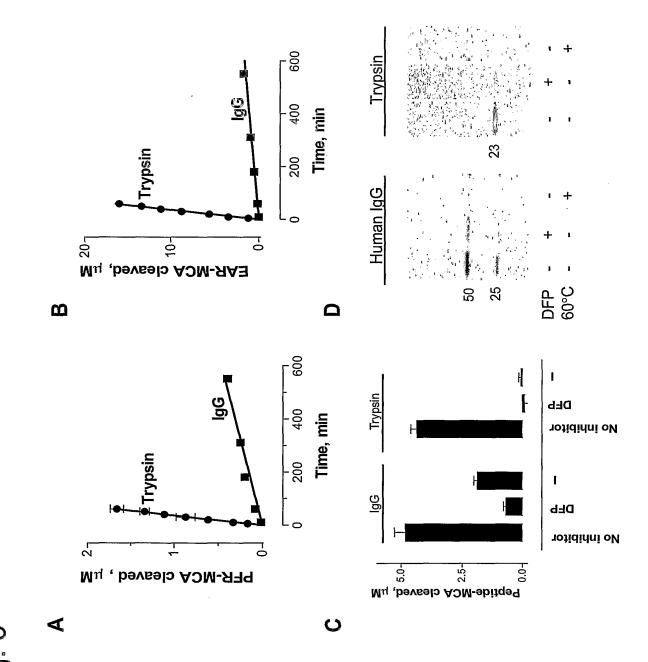
Example of 5: 4'-Carboxybenzo-18-crown-6

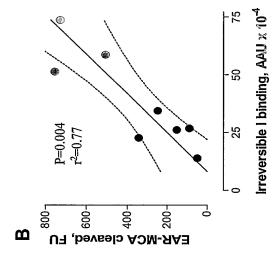
Example of 4: EDTA











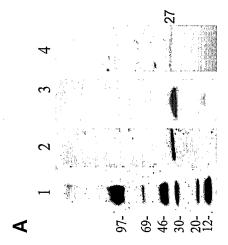
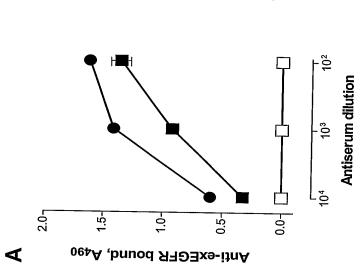
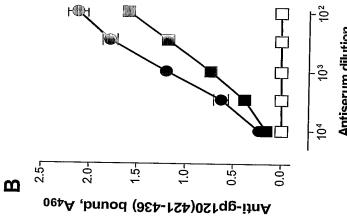


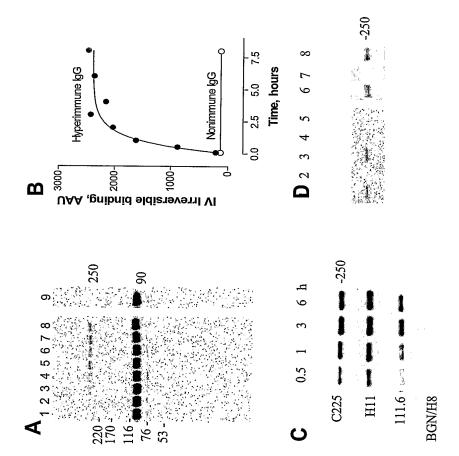
Fig. 10













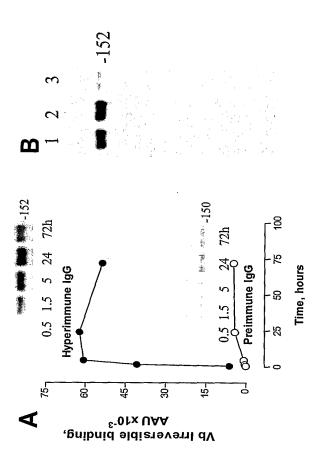


Fig 14

$$A = \frac{12}{12} R_3$$

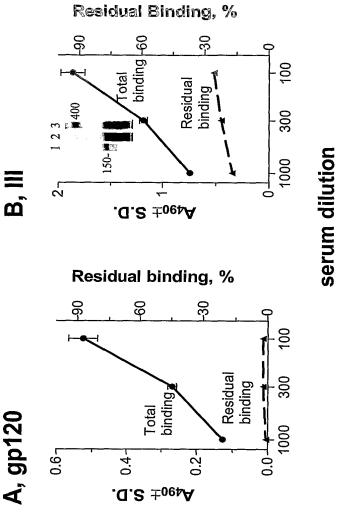
$$A = \frac{12}{12} R_3$$

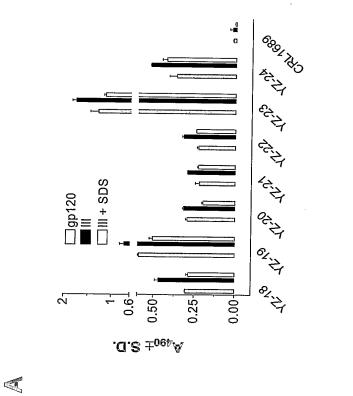
$$A = \frac{12}{12} R_3$$

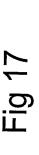
$$A = \frac{12}{140} R_3$$

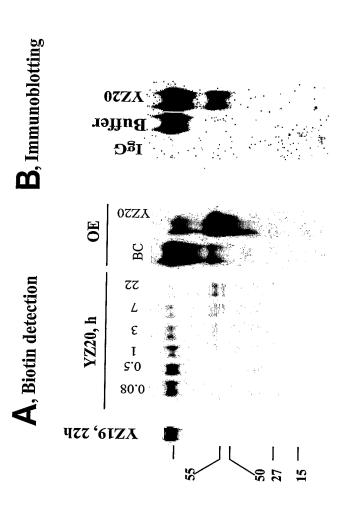
$$A = \frac{140}{140} R_3$$

Fig 15

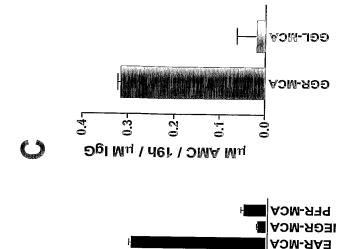






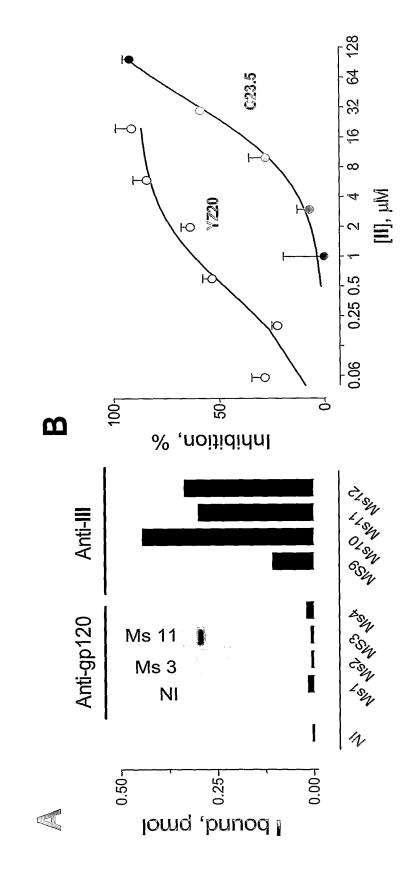






IIW-MCA PAPF-MCA VLK-MCA

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HN NH₂

R-N P-O

R-N P-O

1: R = 6-(D-biotinamido)hexanoyl

2: R = O-succinimidylsuberyl

Lys-Tyr-Leu-Asn-Ser-lle-Leu-Asn-NH₂ O R-His-Ser-Asp-Ala-Val-Phe-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Lys-Gin-Met-Ala-Val—N H

3: R = D-biotinyl

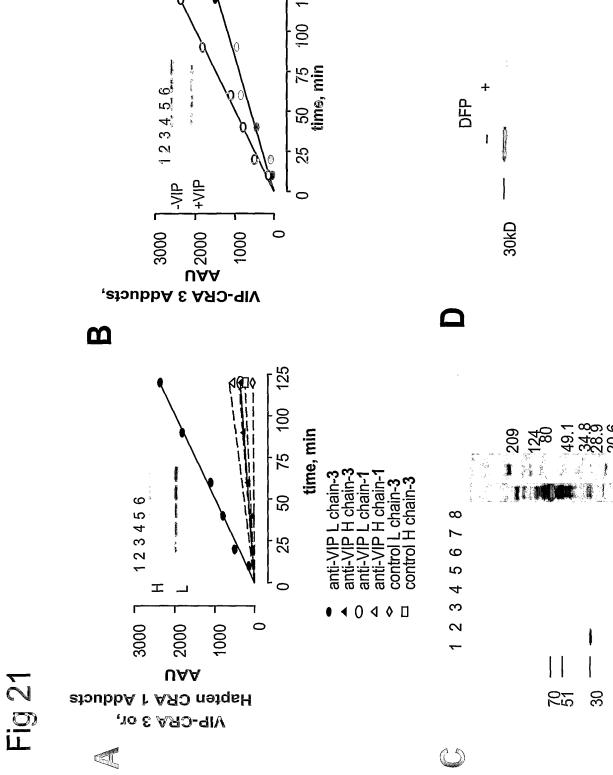
Fmoc-Asn(Trt)—N—

R₁-His-Sei-Asp-Ala-Val-Phe-Thr-Asp-Asn-Tyr-Thr-Arg-Leu-Arg-Lys-Gin-Met-Ala-Val-Lys-Lys-Tyr-Leu-Asn-Sei-Ile-Leu-Asn— Boc tBuO tBuO tBu Pmc Roc - 4a (R₁=Fmoc; R₂=Mtt)

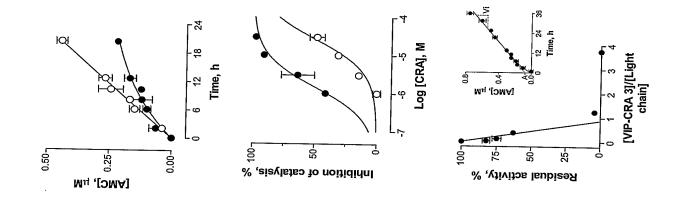
Solid support

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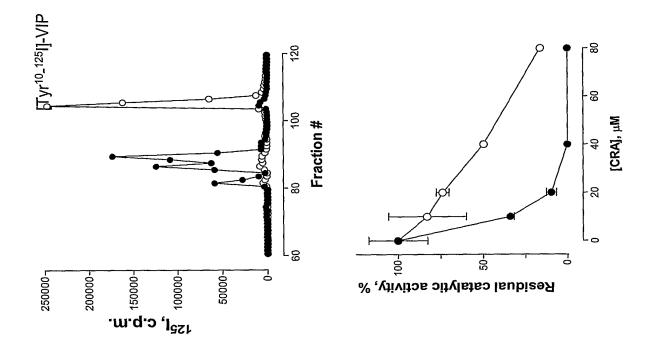




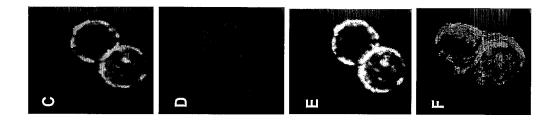




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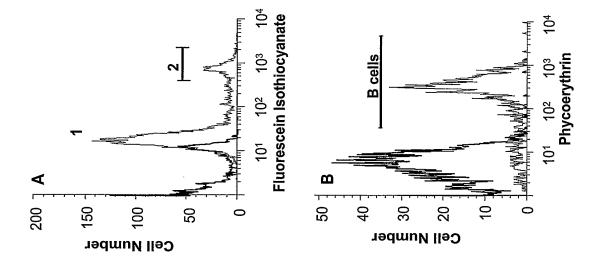
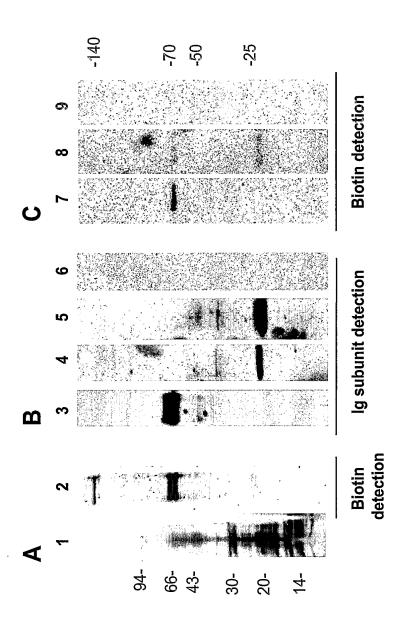


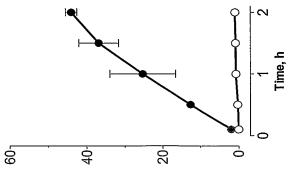
Fig 25

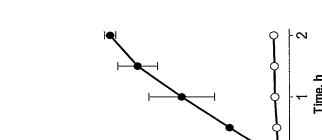


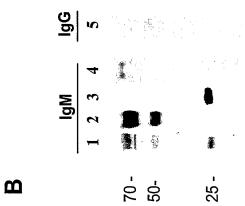


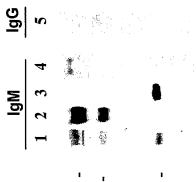


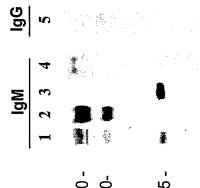


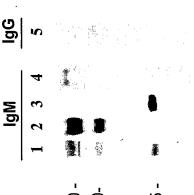


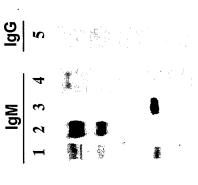


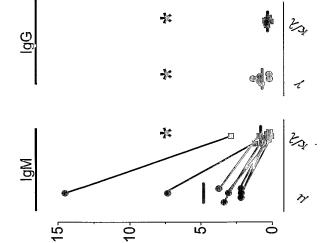






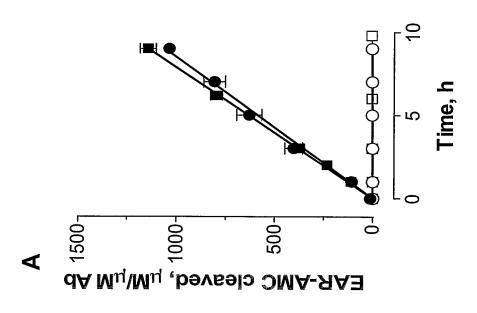


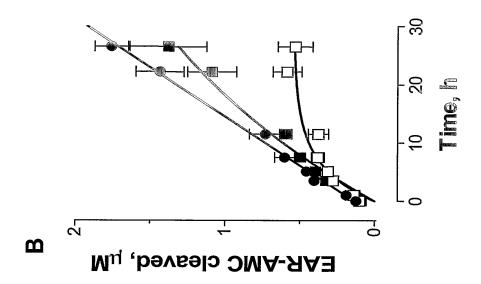




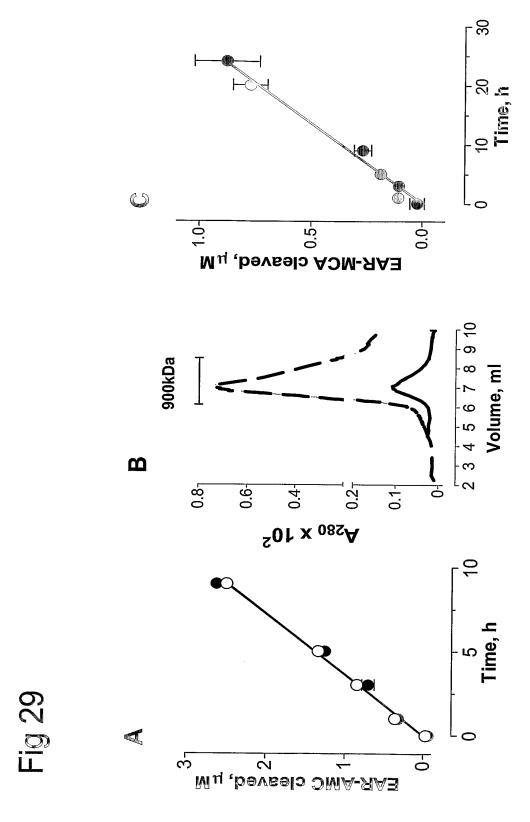
Velocity, AAU/h/ μ M Ab subunit (x10 $^{4-}$

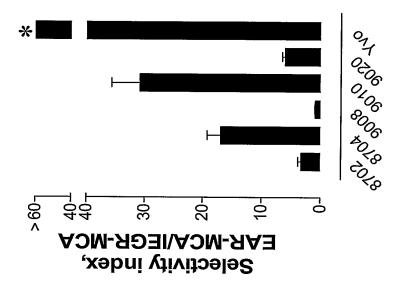
Fig 28





WO 2004/087735 PCT/US2004/009398 32/52

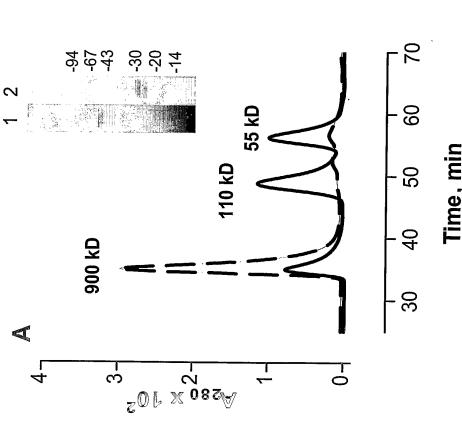




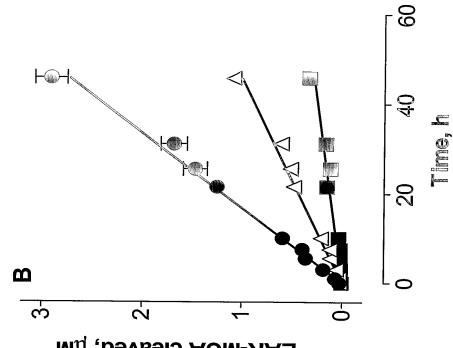
08 10 10 10

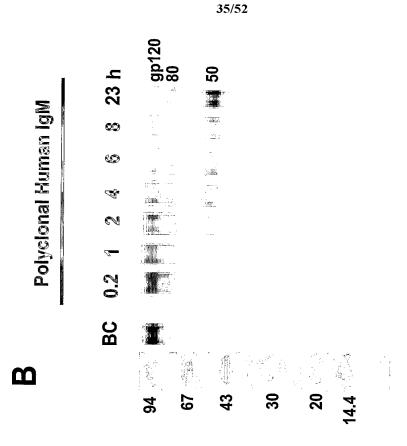
WO 2004/087735

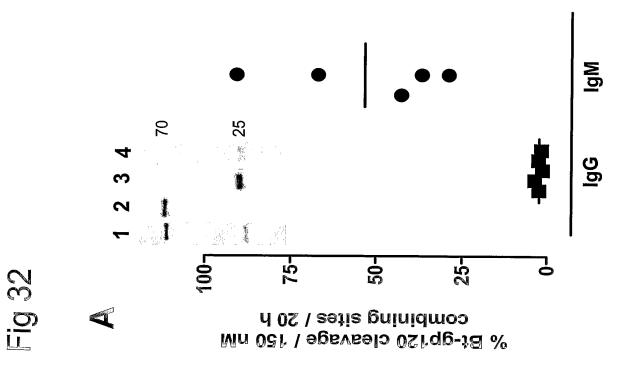


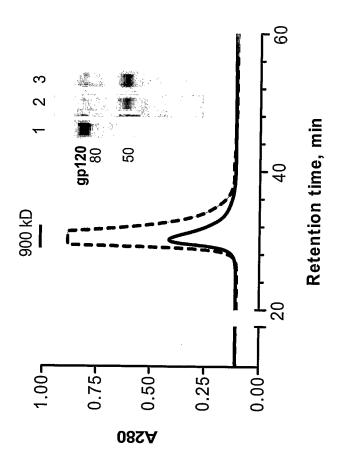




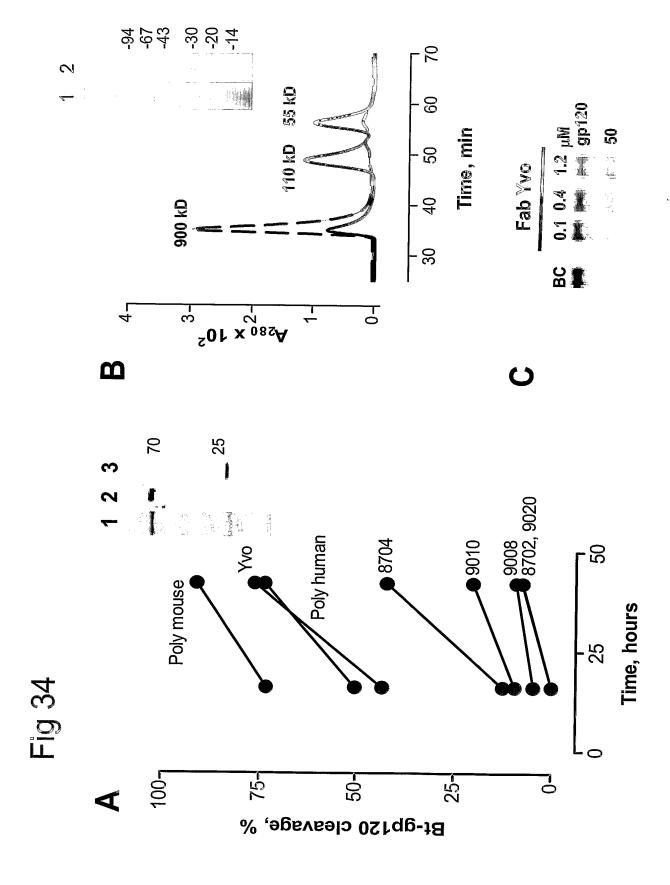




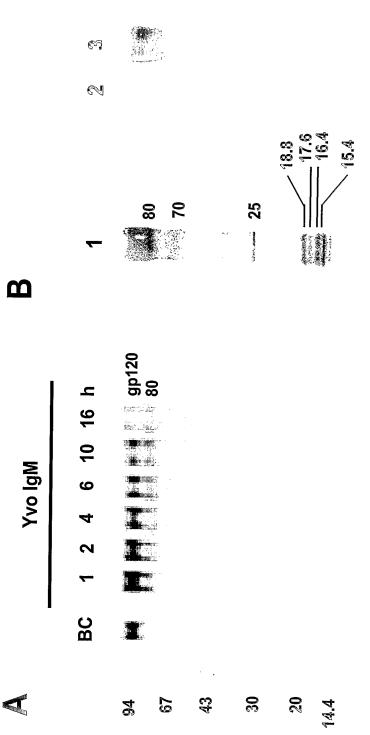




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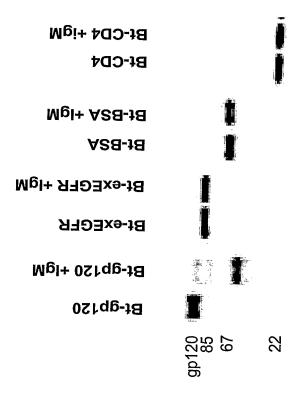
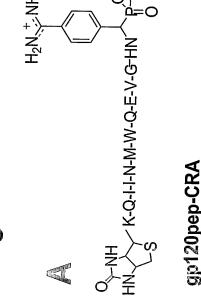
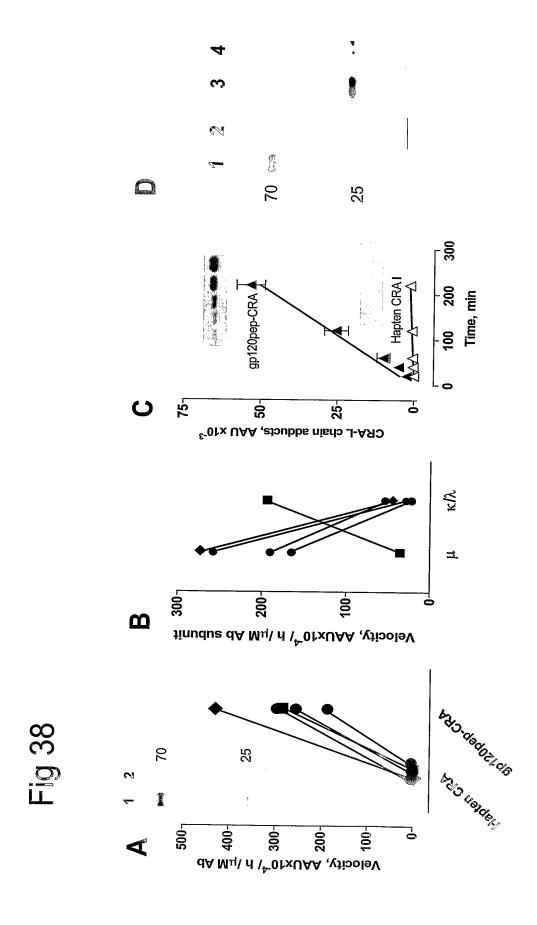


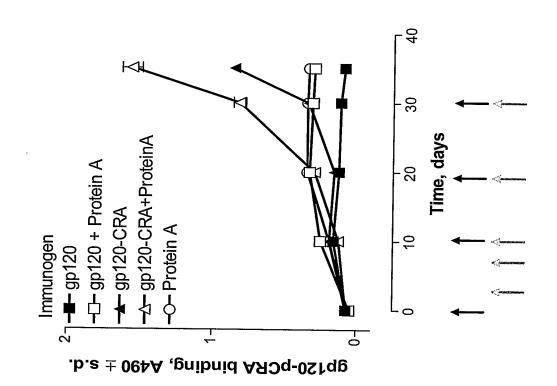
Fig 3

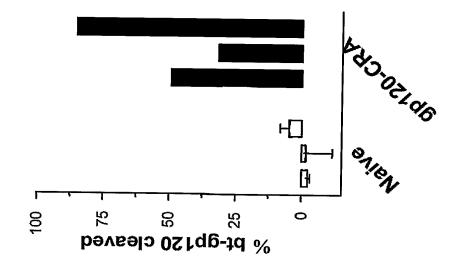


Inhibition of Bt-gp120 cleavage, $\% \pm$ s.d.

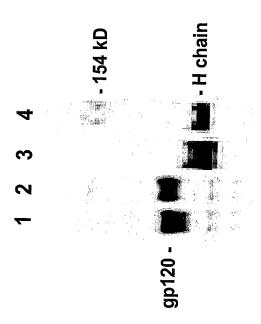


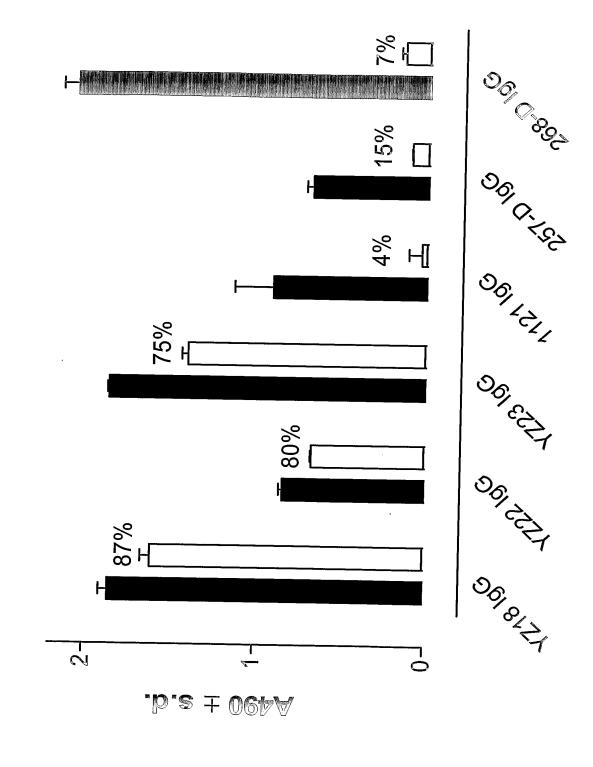






FG 40





-10 42 -10 42

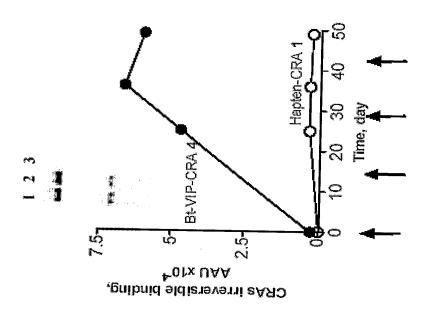
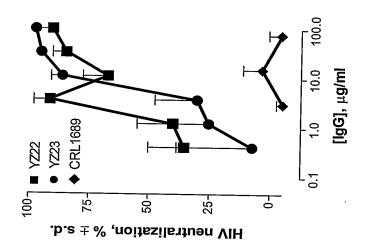
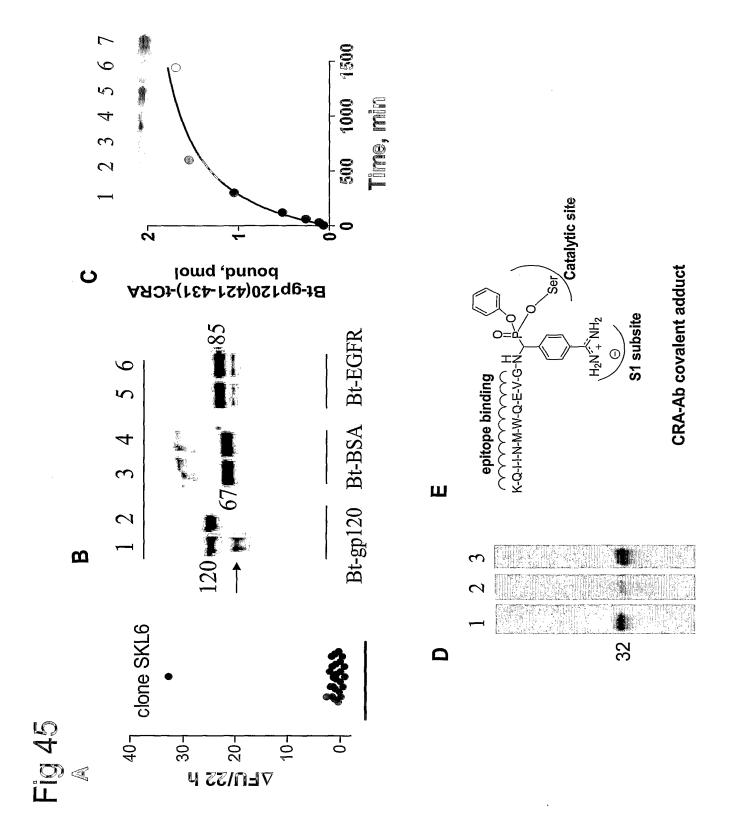
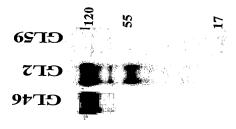


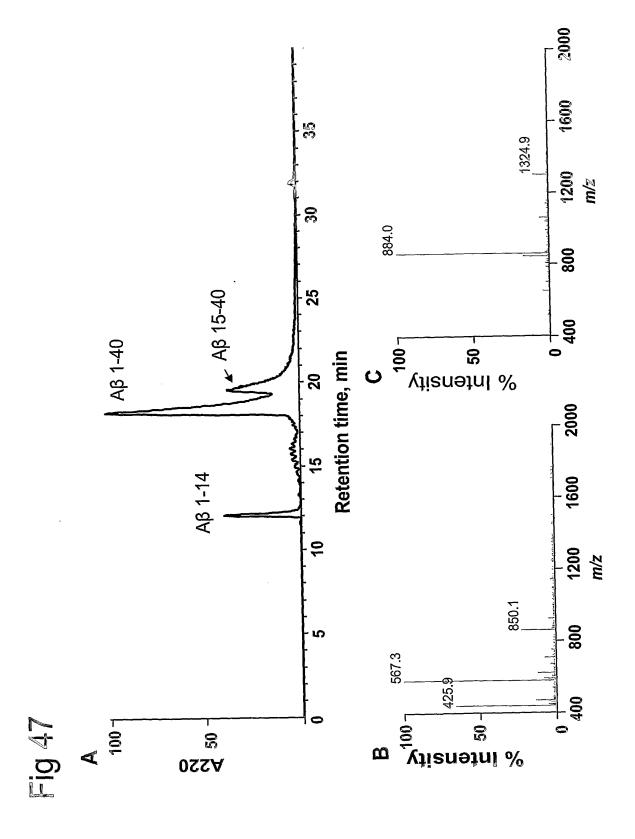
FIG 43











AB17-42-CRAW 4

R-DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA-OH

H2N
$$\bigoplus_{i=0}^{N}$$
NH2

HN $\bigoplus_{i=0}^{N}$ NH2

H20 $\bigoplus_{i=0}^{N}$ HH

H30 $\bigoplus_{i=0}^{N}$ HH

H30

R-HSDAVFTDNYTRLRKQMAVKKYLNSILN **DyruvyI VIP-CRA VIP-CRA 5** R-HSDAVFTDNYTRLRKQMAVKKYLNSILN **VIP-CRA 4**

R--HSDAVFTDNYTRLRKQMAVKKYLNSILN